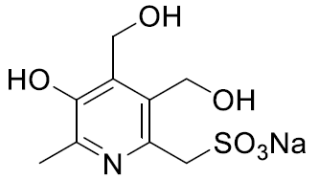
DR-9

SYNTHETIC ROUTE OPTIMIZATION OF SUMEPIRIN ANTIEPILEPTIC DRUG CANDIDATE

M. S. Dzyurkevich, N. V. Shtyrlin, Y. G. Shtyrlin

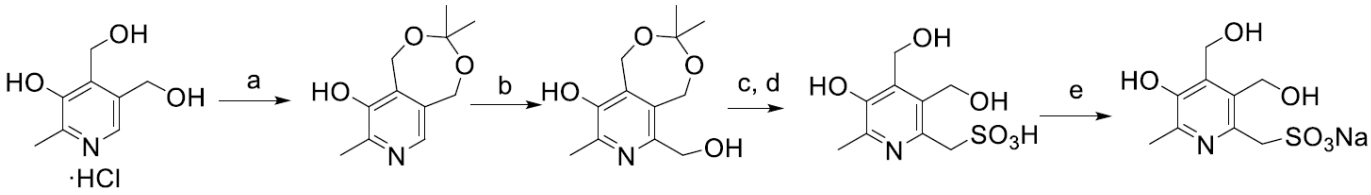
Kazan (Volga region) Federal University, 420008, Russia, Kazan, 18 Kremlevskaya St
E-mail: yurii.shtyrlin@kpfu.ru

Abstract. Epilepsy is one of the most common chronic diseases of the nervous system in the world, which affects both children and adults. 30% of patients with epilepsy are pharmacoresistant.[1] Sumepirin **1** is a novel antiepileptic drug candidate developed in the Scientific and Educational Center of Pharmaceutics of the Kazan Federal University and having pronounced antiseizure effect and improved safety profile. This compound is pyridoxine-based molecule with residue of methanesulfonic acid in the 6th position of pyridoxine ring.



Sumepirin **(1)**

It has successfully passed preclinical studies in the framework of State program of Russian Federation “Development of the Pharmaceutical and Medical Industry” and is planned to undergo the clinical trials. As Sumepirin entered preclinical studies stage an urgent need of the optimization of its method of synthesis arised. As a result of synthetic rout optimization the final synthetic scheme was obtained (Scheme 1).



2 **3** (87%) **4** (94%) **11** (78%) **1** (98%)

Scheme 1. Reagents and conditions: (a) $(CH_3)_2CO$, HCl, 0 °C, 12 h[2]; (b) CH_2O, NaOH, H_2O, 70 °C, 6 h; (c) Na_2SO_3, H_2O, pH = 8.0-9.0, reflux, 5 h; (d) HCl, pH = 1.0, r.t., 0.5 h; (e) NaOH, H_2O, r.t., 0.1 h.

Total yield of the final method of synthesis Sumepirin **1** starting prom pyridoxine hydrochloride was increased from up to 62.5 % in four steps without colon chromatography purification which allows to obtain the target compound with purity of 99.5+% which is especially important for the active ingredient. The method is environment-friendly: at first step reagent (acetone) is used as a solvent and any other step is carried out in water media; good level of atom economy was achieved.

References

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2. Korytnyk W. A seven-membered cyclic ketal of pyridoxol // J Org Chem. – 1962. – Vol. 27, Iss. 10. – P. 3724–3726.

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